(2) *For products containing sulfur identified in § 333.310(e) and (f).*

(i) The labeling states ''Do not use on [bullet] broken skin [bullet] large areas of the skin.''

(ii) The labeling states ''When using this product [bullet] apply only to areas with acne.''

(3) *For products containing any combination identified in § 333.320.* (i) The labeling states ''When using this product [bullet] rinse right away with water if it gets in eyes.''

(ii) The labeling states ''Stop use and ask a doctor [bullet] if skin irritation occurs or gets worse.''

(4) *For products containing benzoyl peroxide identified in § 333.310(a).*

(i) The labeling states ''Do not use if you [bullet] have very sensitive skin [bullet] are sensitive to benzoyl peroxide.''

(ii) The labeling states ''When using this product [bullet] avoid unnecessary sun exposure and use a sunscreen [bullet] avoid contact with the eyes, lips, and mouth [bullet] avoid contact with hair and dyed fabrics, which may be bleached by this product [bullet] skin irritation may occur, characterized by redness, burning, itching, peeling, or possibly swelling. Irritation may be reduced by using the product less frequently or in a lower concentration.''

(iii) The labeling states ''Stop use and ask a doctor if [bullet] irritation becomes severe.''

(d) *Directions.* The labeling of the product contains the following information under the heading ''Directions'':

(1) *For products applied containing any ingredient identified in § 333.310.* The labeling states ''[bullet] clean the skin thoroughly before applying this product [bullet] cover the entire affected area with a thin layer one to three times daily [bullet] because excessive drying of the skin may occur, start with one application daily, then gradually increase to two or three times daily if needed or as directed by a doctor [bullet] if bothersome dryness or peeling occurs, reduce application to once a day or every other day.''

(2) *For products applied and left on the skin containing benzoyl peroxide identified in § 333.310(a).*

(i) The labeling states the directions in paragraph (d)(1) of this section.

(ii) The labeling states ''[bullet] if going outside, apply sunscreen after using this product. If irritation or sensitivity develops, stop use of both products and ask a doctor.''

(3) *For products applied and removed from the skin containing any ingredient identified in § 333.310.* Products, such as soaps and masks, may be applied and removed and should include appropriate directions. All products containing benzoyl peroxide should include the directions in paragraph (d)(2)(ii) of this section.

(4) *Optional directions.* In addition to the required directions in paragraphs (d)(1) and (d)(2) of this section, the product may contain the following optional labeling: ''*Sensitivity Test for a New User.* Apply product sparingly to one or two small affected areas during the first 3 days. If no discomfort occurs, follow the directions stated (select one of the following: 'elsewhere on this label,' 'above,' or 'below').''

PART 335—ANTIDIARRHEAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—General Provisions

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AUTHORITY: 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

SOURCE: 68 FR 18881, April 17, 2003, unless otherwise noted.

Subpart A—General Provisions

§ 335.1 Scope.

(a) An over-the-counter antidiarrheal drug product in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this part and each general condition established in § 330.1 of this chapter.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to chapter I of title 21 unless otherwise noted.

§ 335.3 Definitions.

As used in this part:

(a) *Antidiarrheal.* A drug that can be shown by objective measurement to treat or control (stop) the symptoms of diarrhea.

(b) *Diarrhea.* A condition characterized by increased frequency of loose, watery stools (three or more daily) during a limited period (24 to 48 hours), usually with no identifiable cause.

(c) *Travelers' diarrhea.* A subset of diarrhea occurring in travelers that is most commonly caused by an infectious agent.

[68 FR 18881, April 17, 2003, as amended at 69 FR 26302, May 12, 2004]

Subpart B—Active Ingredients

§ 335.10 Antidiarrheal active ingredients.

The active ingredient of the product consists of any one of the following when used within the dosage limits established for each ingredient in § 335.50(d):

(a) Bismuth subsalicylate.

(b) Kaolin.

Subpart C—Labeling

§ 335.50 Labeling of antidiarrheal drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product either as an ''antidiarrheal'' or ''for diarrhea.''

(b) *Indications.* The labeling of the product states, under the heading ''Use,'' one or more of the phrases listed in this paragraph (b), as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this paragraph (b) may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *For products containing bismuth subsalicylate identified in § 335.10(a).* The labeling states [select one of the following: ''controls'' or ''relieves''] [select one or both of the following: ''diarrhea'' or ''travelers' diarrhea'']. If both ''diarrhea'' and ''travelers' diarrhea'' are selected, each shall be preceded by a bullet in accordance with § 201.66(b)(4) and (d)(4) of this chapter and the heading ''Uses'' shall be used.

(2) *For products containing kaolin identified in § 335.10(b).* The labeling states ''helps firm stool within 24 to 48 hours''.

(3) *Additional indications*—(i) When any additional indications are used, the heading ''Uses'' shall be used and each listed use shall be preceded by a bullet in accord with § 201.66(b)(4) of this chapter.

(ii) In addition to the indication in paragraph (b)(1) of this section, one or both of the following may be used for products containing bismuth subsalicylate in § 335.10(a): ''[bullet] reduces number of bowel movements'' ''[bullet] helps firm stool''.

(c) *Warnings.* The labeling of the product contains the following warnings under the heading ''Warnings'':

(1) *For products containing any ingredient identified in § 335.10.* (i) ''Do not use if you have [bullet] bloody or black stool''.

(ii) ''Ask a doctor before use if you have [bullet] fever [bullet] mucus in the stool''.

(2) *For products containing bismuth subsalicylate identified in § 335.10(a).* (i) The following shall appear in accordance with § 201.66(c)(5)(ii) of this chapter.

(A) The Reye's syndrome warning in § 201.314(h) of this chapter.

(B) ''Allergy alert: Contains salicylate. Do not take if you are [bullet] allergic to salicylates (including aspirin), [bullet] taking other salicylate products''.

(ii) ''Do not use if you have [bullet] an ulcer [bullet] a bleeding problem''.

(iii) ''Ask a doctor or pharmacist before use if you are taking any drug for [bullet] anticoagulation (thinning the blood) [bullet] diabetes [bullet] gout [bullet] arthritis''.

(iv) ''When using this product a temporary, but harmless, darkening of the stool and/or tongue may occur''.

(v) ''Stop use and ask a doctor if [bullet] symptoms get worse [bullet] ringing in the ears or loss of hearing occurs [bullet] diarrhea lasts more than 2 days''.

(3) *For products containing kaolin identified in § 335.10(b).* (i) ''Ask a doctor or pharmacist before use if you are taking any other drugs. Try to use at least 3